

California Antimicrobial Resistance Laboratory Network:
Candida auris: Emergence, Laboratory Identification,
and Public Health Response
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Candida auris: Emergence, Laboratory Identification, and Public Health Response

- Describe the epidemiology of *C. auris*
- Discuss infection control and public health response to *C. auris* cases
- Describe laboratory considerations for *C. auris* identification
- Discuss role of the California AR Lab Network in *C. auris* surveillance

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Candida auris Emergence, Laboratory Identification, and Public Health Response

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Mycotic Diseases Branch, Centers for Disease Control and Prevention

CA DPH Webinar

6/27/2017





What the public thinks



9,000 DRUG-RESISTANT INFECTIONS PER YEAR

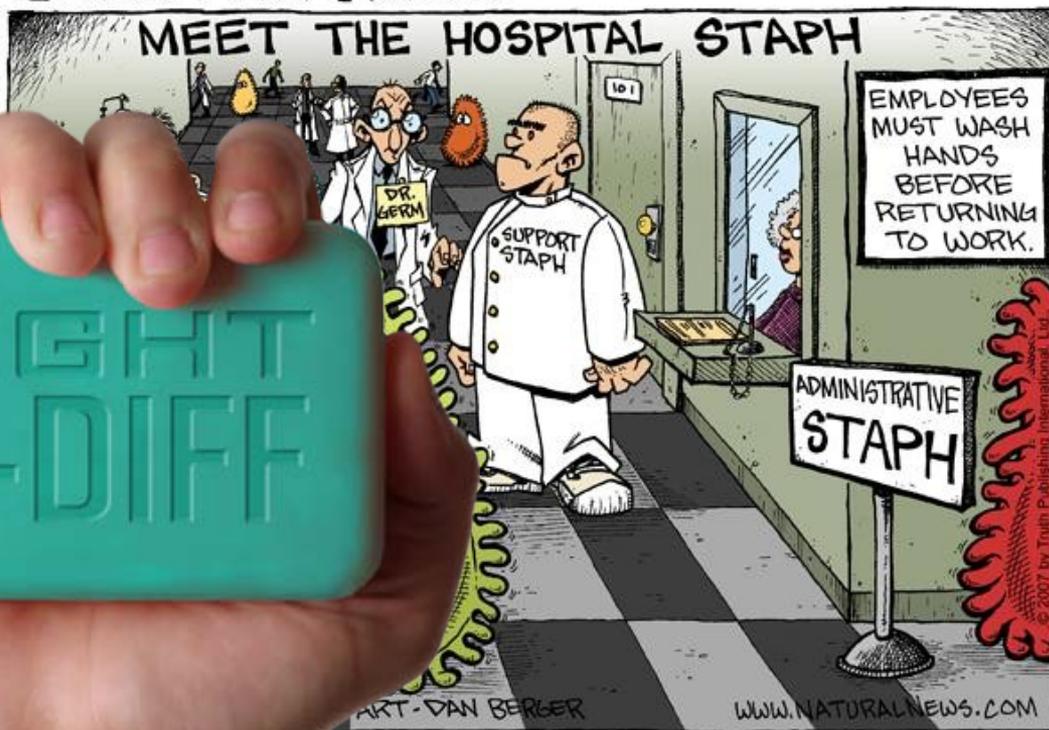
CA
KLEB

THREAT LEVEL
SERIOUS

This bacteria is a serious concern and requires immediate and sustained action to ensure the problem is resolved.

The infographic features a green virus-like icon at the top left, a yellow warning triangle at the bottom left, and a background of pink, oval-shaped bacteria. The text '9,000 DRUG-RESISTANT INFECTIONS PER YEAR' is in large green and white letters. Below it, 'THREAT LEVEL SERIOUS' is written in white on a dark background, with three yellow circles to the right. At the bottom, a white box contains the text 'This bacteria is a serious concern and requires immediate and sustained action to ensure the problem is resolved.'

COUNTERTHINK



What the healthcare professionals think



THERE'S A FUNGUS
AMONG US.

Fungi can cause serious, invasive infections and be HAIs

- **Candidemia**

Most common healthcare-associated BSI in a recent US point prevalence study

- Incidence of 5-15/100,000
- 30-50% mortality



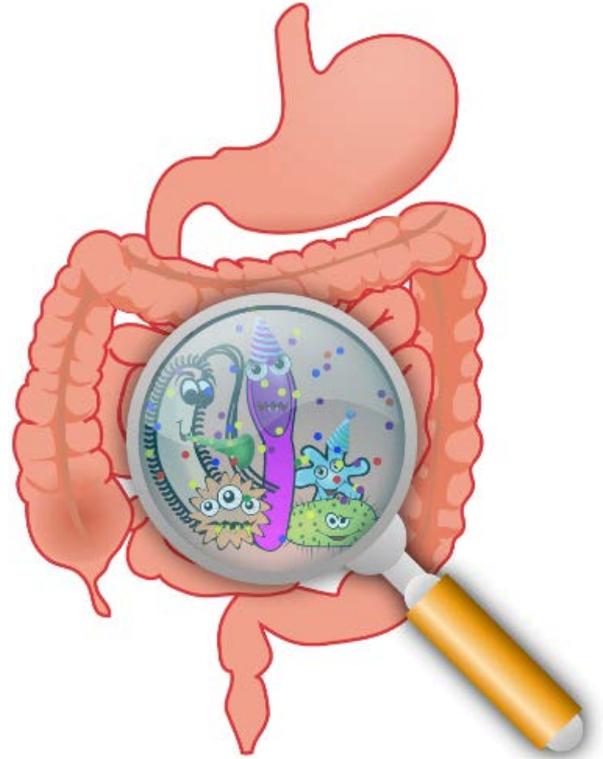
Risk Factors for Candidemia (“the other *C. diff*”)

- Broad-spectrum antibiotic use
- Immune compromise
- Prolonged ICU stay
- Abdominal surgery
- Central lines

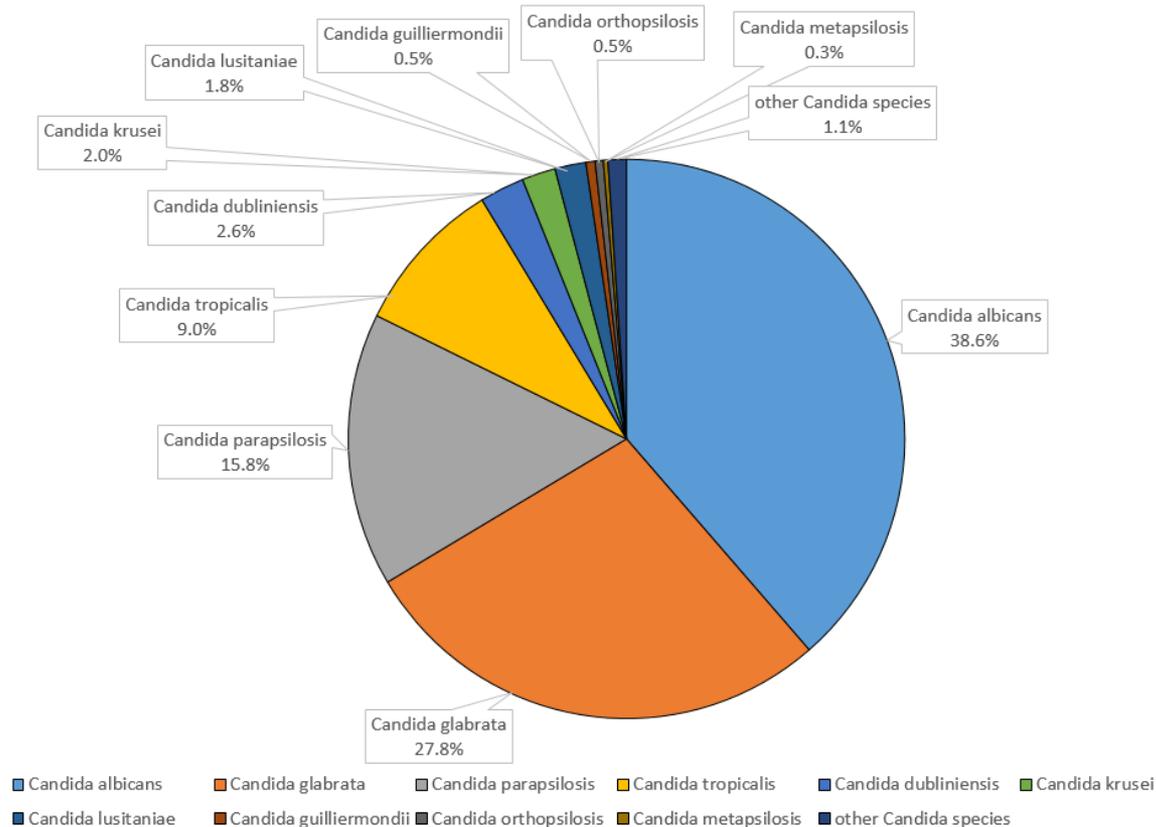


Source of infection

- **Conventional wisdom:**
autoinfection with host gut flora
- Transmission in hospital environments not thought to be common
- Outbreaks rare



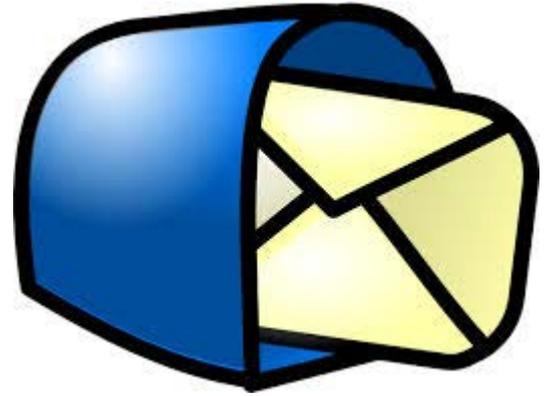
Bloodstream *Candida* species distribution, EIP Surveillance, U.S. 2008-2016 (n=~7000 isolates)





**Why We Care About an Obscure *Candida*
Species called *C. auris***

It always starts with an email...



February 2015

- Pakistani colleagues concerned about outbreak of *Saccharomyces cerevisiae* infections
 - 22 isolates over 2 months
 - 8 bloodstream, 3 burn wounds, 10 urine, 1 catheter tip

But it wasn't *Saccharomyces*...

- A commercial test kit had been used for identification
- DNA sequencing revealed that the isolates were *Candida auris*



Discovery of *C. auris*—2009

ORIGINAL ARTICLE

***Candida auris* sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital**

Kazuo Satoh^{1,2}, Koichi Makimura^{1,3}, Yayoi Hasumi¹, Yayoi Nishiyama¹, Katsuhisa Uchida¹ and Hideyo Yamaguchi¹

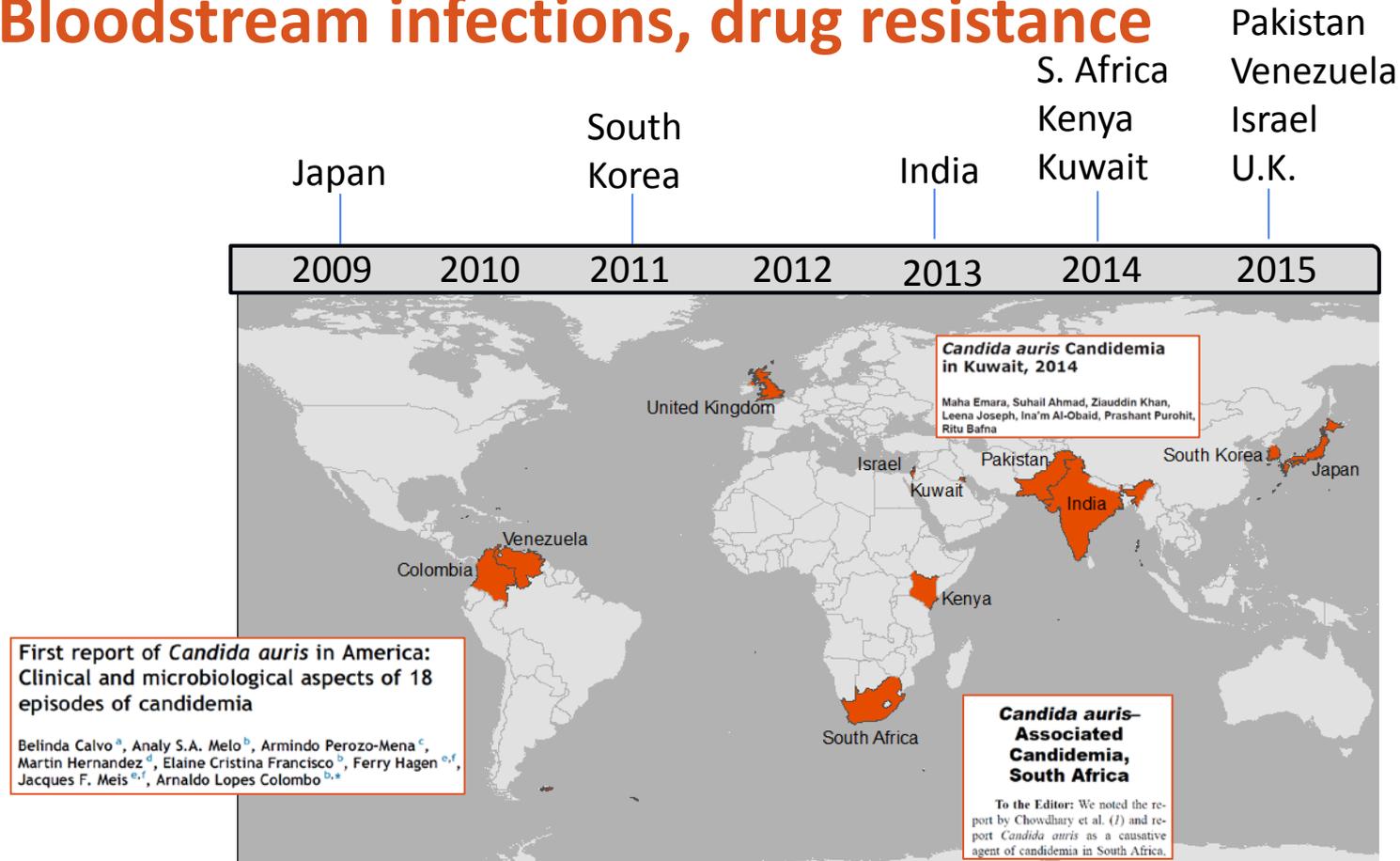
¹Teikyo University Institute of Medical Mycology, 359 Otsuka, Hachioji, Tokyo 192-0395, ²Japan Health Sciences Foundation, 13-4 Nihonbashi-Kodenmacho, Chuo-ku, Tokyo 103-0001 and ³Genome Research Center, Graduate School of Medicine and Faculty of Medicine, Teikyo University, Otsuka 359, Hachioji, Tokyo 192-0395, Japan

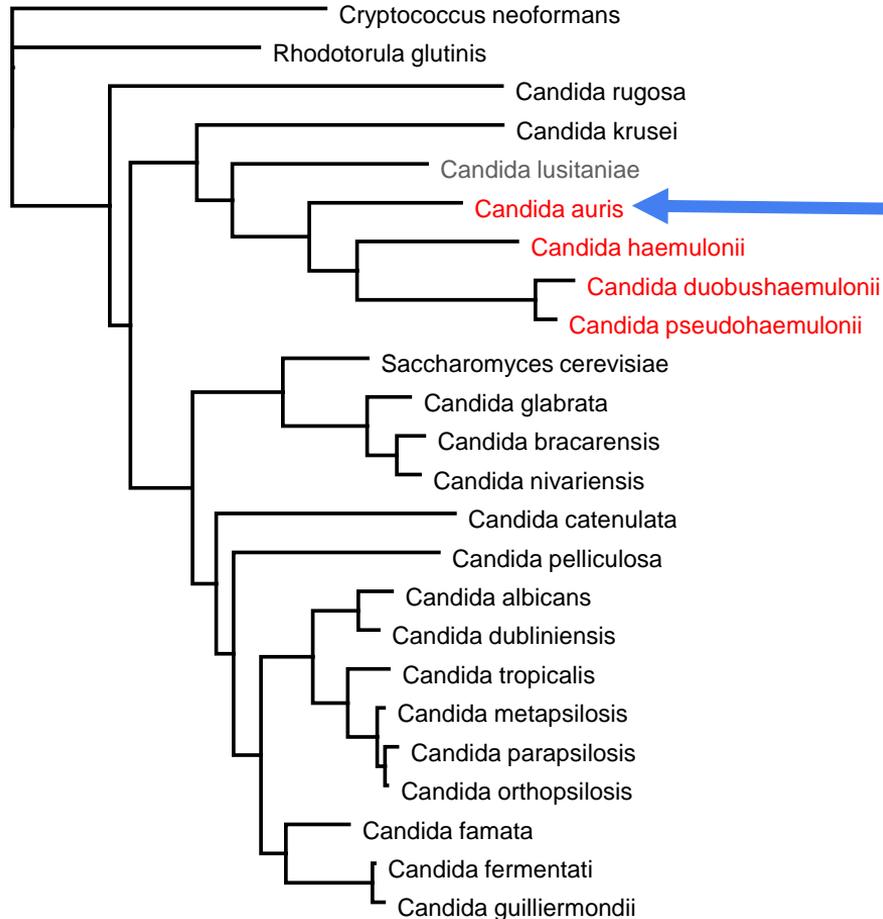
Auris is Latin for ear



Rapid Emergence Since 2009

Bloodstream infections, drug resistance

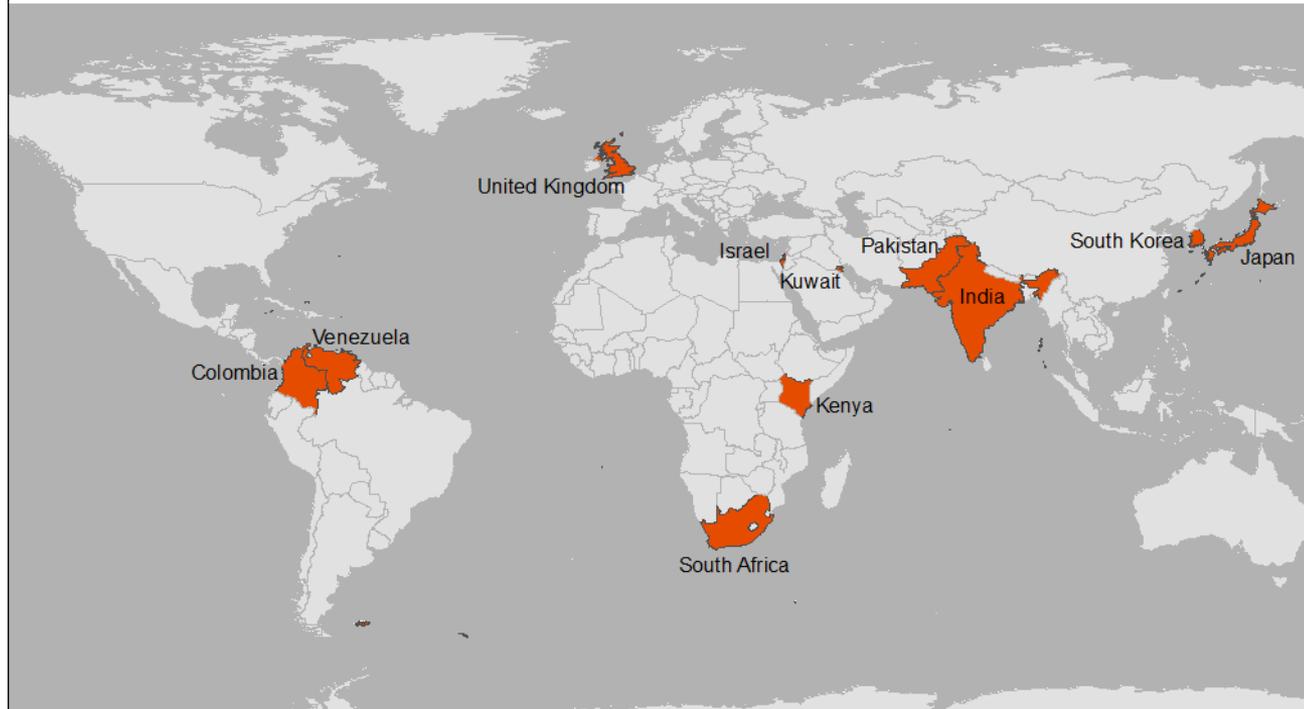




Closely related to other *Candida* species known for antifungal resistance

*Cauris*likes
 high salinity
 high temperatures (>40C)

CDC Formed an International Collaboration



Major antifungal resistance was seen

1



93% resistant to fluconazole
54% resistant to voriconazole

2



7% resistant to
echinocandins

3



35% resistant to
amphotericin B

- 41% isolates multidrug resistant
- 4% resistant to all three classes

By way of comparison: *Candida glabrata*

1



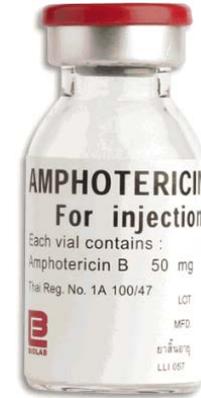
11% resistant to fluconazole

2



1-6% resistant to echinocandins

3



<1 % resistant to amphotericin B

- **1-3% isolates multidrug resistant**
- **0 pan resistant isolates**

Healthy Skepticism

- Was *C. auris* with us all along?
- Maybe newer diagnostic methods responsible for supposed emergence
 - MALDI-TOF
 - DNA sequencing
- Most systems misidentify as *Candida haemulonii* or other species

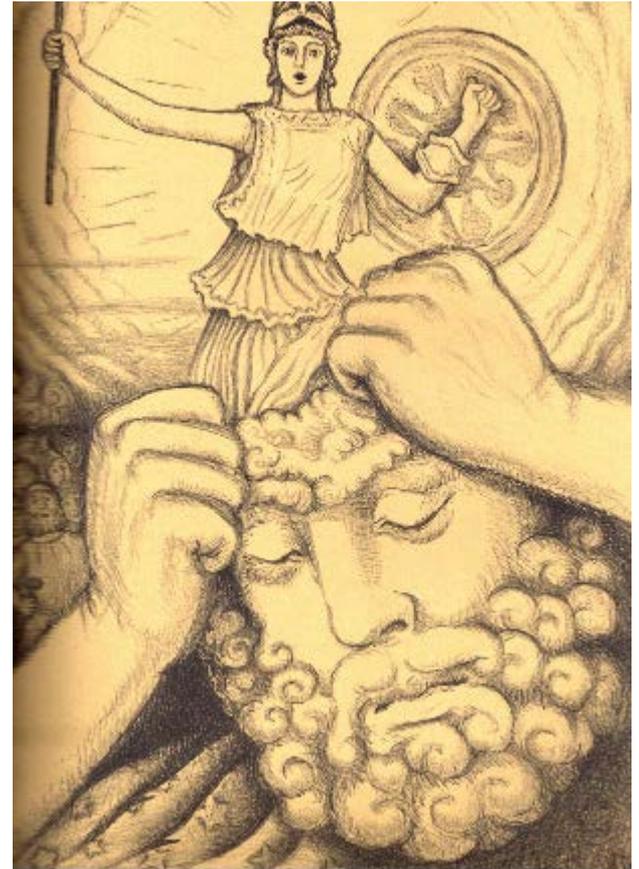


Not Just Improved Detection

- EIP Candidemia Surveillance Program
 - >7000 *Candida* isolates collected in U.S. 2008 –2016
 - No *C. auris*
- SENTRY and ARTEMIS programs (private collections from 4 continents)
 - >30,000 *Candida* isolates from 1996-2015
 - No *C. auris* before 2009
- Earliest known isolate of *C. auris* has been recorded in S. Korea in 1996

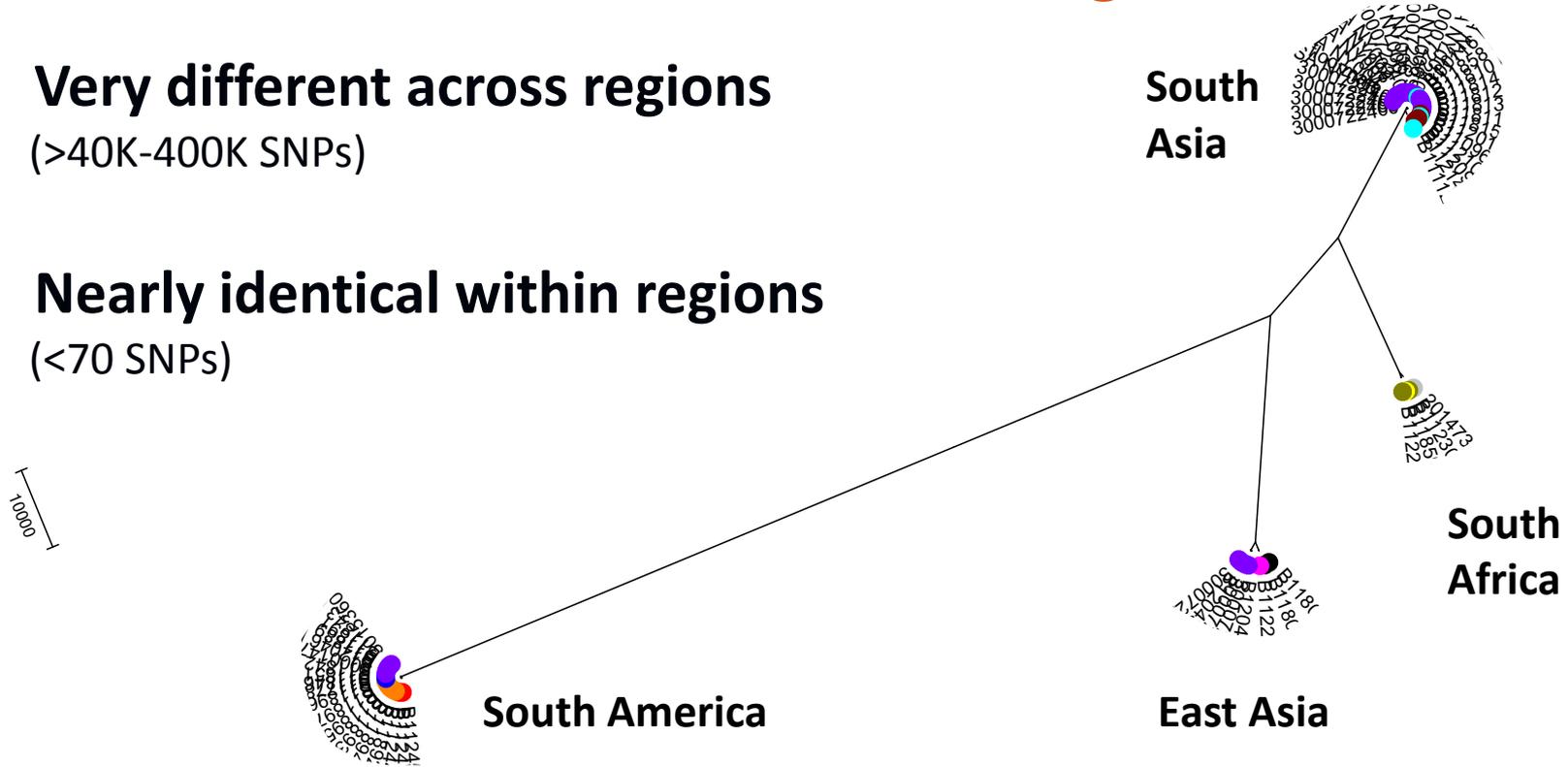
How Did *C. auris* Emerge?

- Global spread of single epidemic strain? (e.g., through food or medical product)
- Many introductions from the environment or other sources?
- Whole-genome sequencing (WGS) provides remarkable but puzzling results



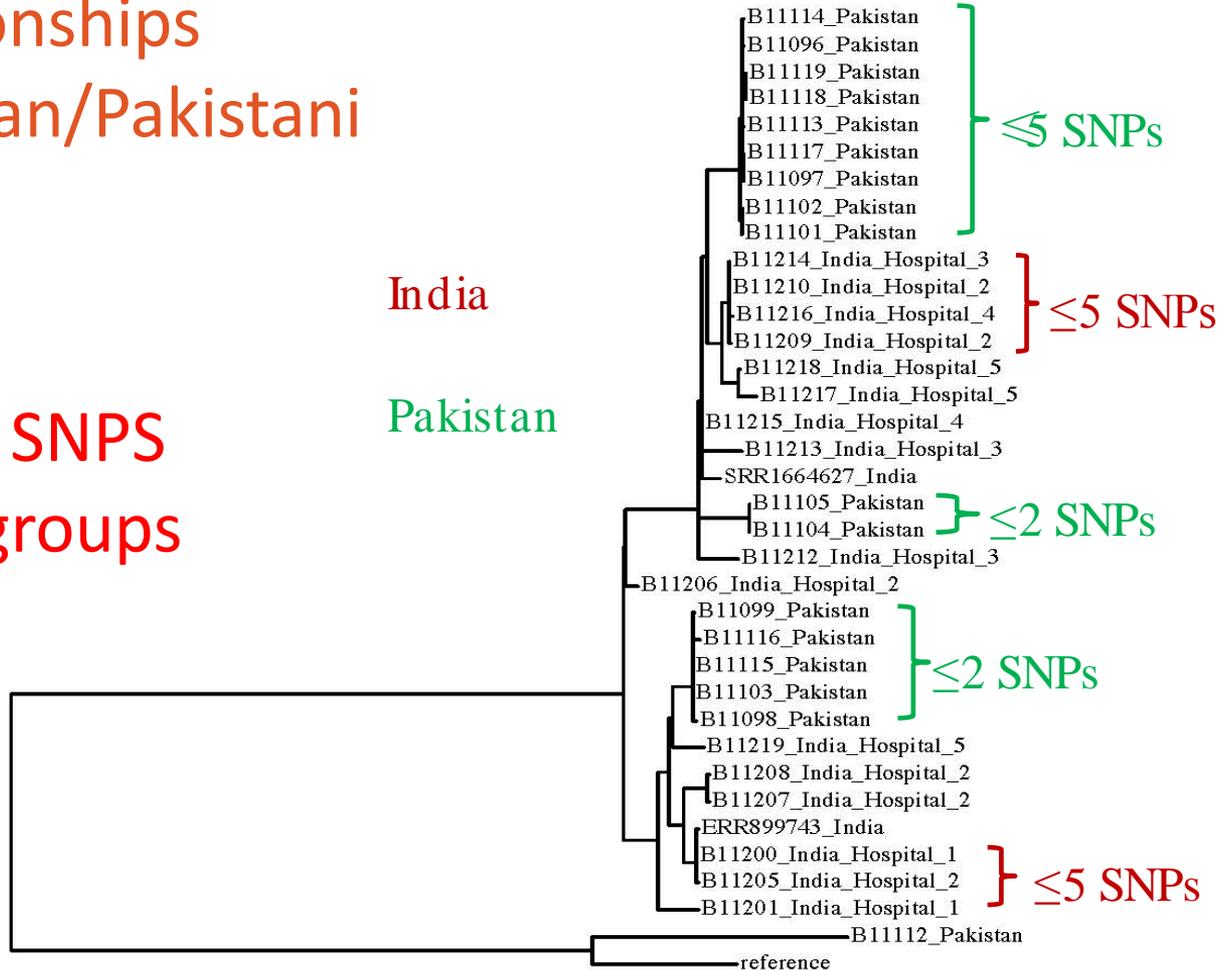
WGS of 47 isolates from 4 world regions

- **Very different across regions**
(>40K-400K SNPs)
- **Nearly identical within regions**
(<70 SNPs)



WGS relationships among Indian/Pakistani strains

But only 70 SNPs
within the groups



But This Really Got Our Attention...

- *C. auris* outbreak in a UK hospital
- 9 *C. auris* bloodstream infections
- >40 people colonized
- Clear patient-to-patient transmission



Hard to Control

- Contact precautions
- Screening for colonization
- Chlorhexidine bathing
- Cleaning room with bleach 3X/day
- Terminal cleaning with higher concentration bleach
- Eventually closed unit



C. auris cultured from many hospital surfaces

CDC Clinical Alert to Healthcare Facilities – June 2016

Fungal Diseases

Fungal Diseases	
Types of Fungal Diseases	-
Aspergillosis	+
Blastomycosis	+
Candidiasis	-
Oropharyngeal / Esophageal Candidiasis	
Genital / vulvovaginal candidiasis	
Invasive candidiasis	
<i>Candida auris</i> Q&A	
<i>Candida auris</i> Alert	
Coccidioidomycosis	+
<i>C. neoformans</i> Infection	+
<i>C. gattii</i> Infection	+
Fungal Eye Infections	+

[CDC](#) > [Fungal Diseases](#) > [Types of Fungal Diseases](#) > [Candidiasis](#)

Clinical Alert to U.S. Healthcare Facilities



Global Emergence of Invasive Infections Caused by the Multidrug-Resistant Yeast *Candida auris*

Summary: The Centers for Disease Control and Prevention (CDC) has received reports from international healthcare facilities that *Candida auris*, an emerging multidrug-resistant (MDR) yeast, is causing invasive healthcare-associated infections with high mortality. Some strains of *C. auris* have elevated minimum inhibitory concentrations (MICs) to the three major classes of antifungals, severely limiting treatment options. *C. auris* requires specialized methods for identification and could be misidentified as another yeast when relying on traditional biochemical methods. CDC is aware of one isolate of *C. auris* that was detected in the United States in 2013 as part of ongoing surveillance. Experience outside the United States suggests that *C. auris* has high potential to cause outbreaks in healthcare facilities. Given the occurrence of *C. auris* in nine countries on four continents since 2009, CDC is alerting U.S. healthcare facilities to be on the lookout for *C. auris* in patients.

Background

Candida auris is an emerging multidrug-resistant (MDR) yeast that can cause invasive infections and is associated with high mortality. It was first described in 2009 after being isolated from external ear discharge of a patient in Japan¹. Since the 2009 report, *C. auris* infections, specifically fungemia, have been reported from South Korea², India³, South Africa⁴, and Kuwait⁵. Although published reports are not available, *C. auris* has also been identified in Colombia, Venezuela, Pakistan, and the United Kingdom.

It is unknown why *C. auris* has recently emerged in so many different locations. Molecular typing of strains performed by CDC suggests isolates are highly related within a country, but highly distinct between continents⁶. The earliest known infection with *C. auris* based on retrospective testing of

C. auris in the US

- As of August 31, we had heard about 7 cases
- All retrospectively found except for 1



Morbidity and Mortality Weekly Report

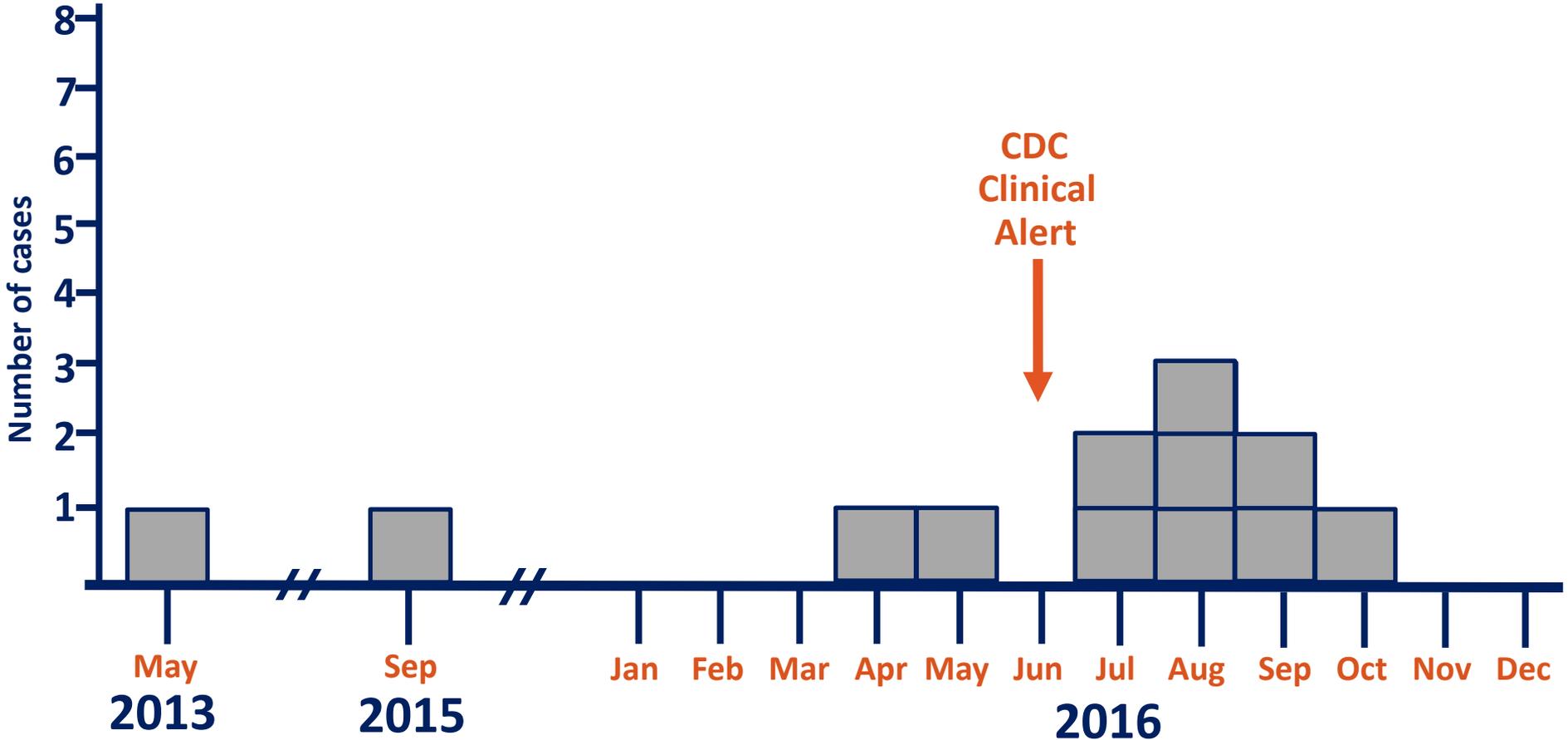
Early Release / Vol. 65

November 4, 2016

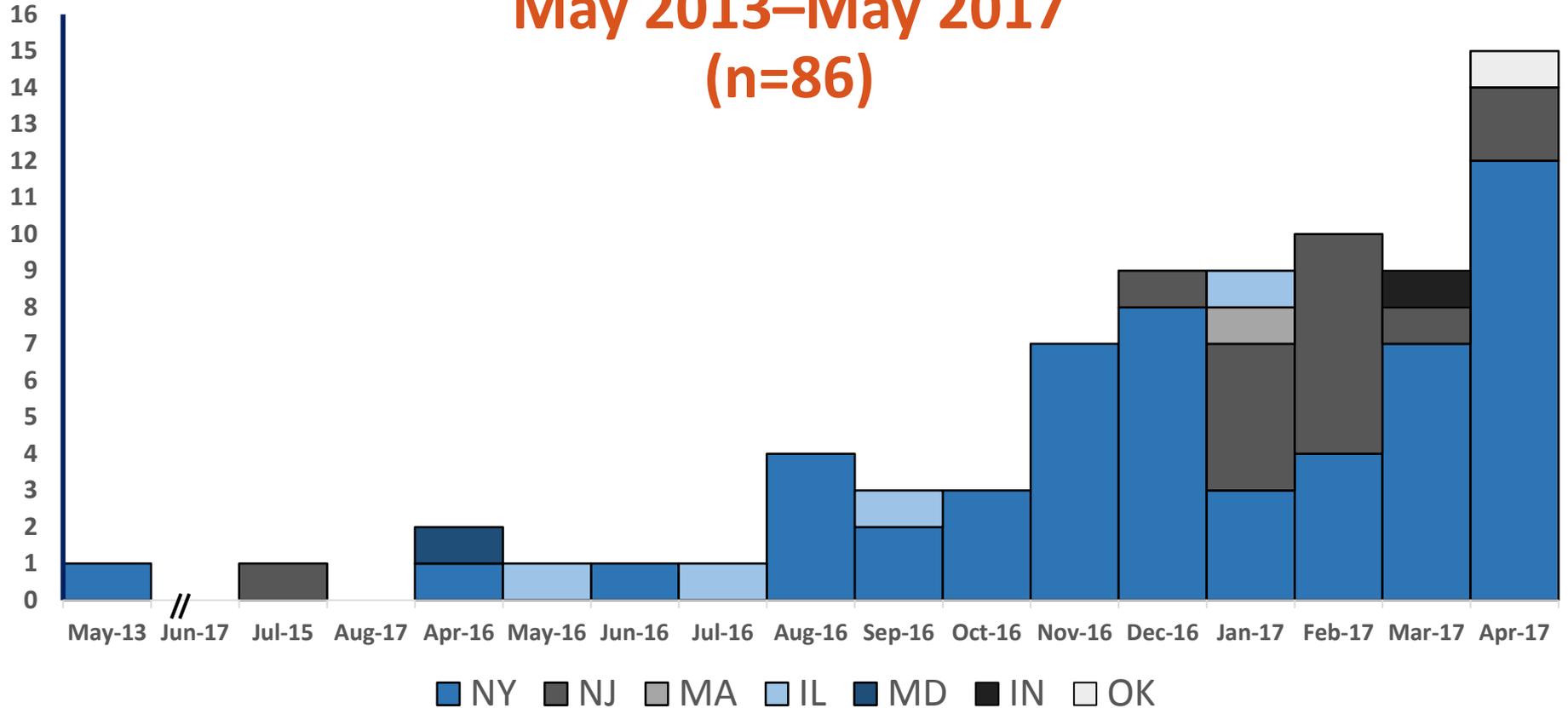
Investigation of the First Seven Reported Cases of *Candida auris*, a Globally Emerging Invasive, Multidrug-Resistant Fungus — United States, May 2013–August 2016

Snigdha Vallabhaneni, MD¹; Alex Kallen, MD²; Sharon Tsay, MD^{1,3}; Nancy Chow, PhD¹; Rory Welsh, PhD¹; Janna Kerins, VMD^{3,4}; Sarah K. Kemble, MD⁴; Massimo Pacilli, MS⁴; Stephanie R. Black, MD⁴; Emily Landon, MD⁵; Jessica Ridgway, MD⁵; Tara N. Palmore, MD⁶; Adrian Zelzany, PhD⁶; Eleanor H. Adams, MD⁷; Monica Quinn, MS⁷; Sudha Chaturvedi, PhD⁷; Jane Greenko, MPH⁷; Rafael Fernandez, MPH⁷; Karen Southwick, MD⁷; E. Yoko Furuya, MD⁸; David P. Calfee, MD⁹; Camille Hamula, PhD¹⁰; Gopi Patel, MD¹⁰; Patricia Barrett, MSD¹¹; Patricia Lafaro¹²; Elizabeth L. Berkow, PhD¹; Heather Moulton-Meissner, PhD²; Judith Noble-Wang, PhD²; Ryan P. Fagan, MD²; Brendan R. Jackson, MD¹; Shawn R. Lockhart, PhD¹; Anastasia P. Litvintseva, PhD¹; Tom M. Chiller, MD¹

12 cases reported by October 2016



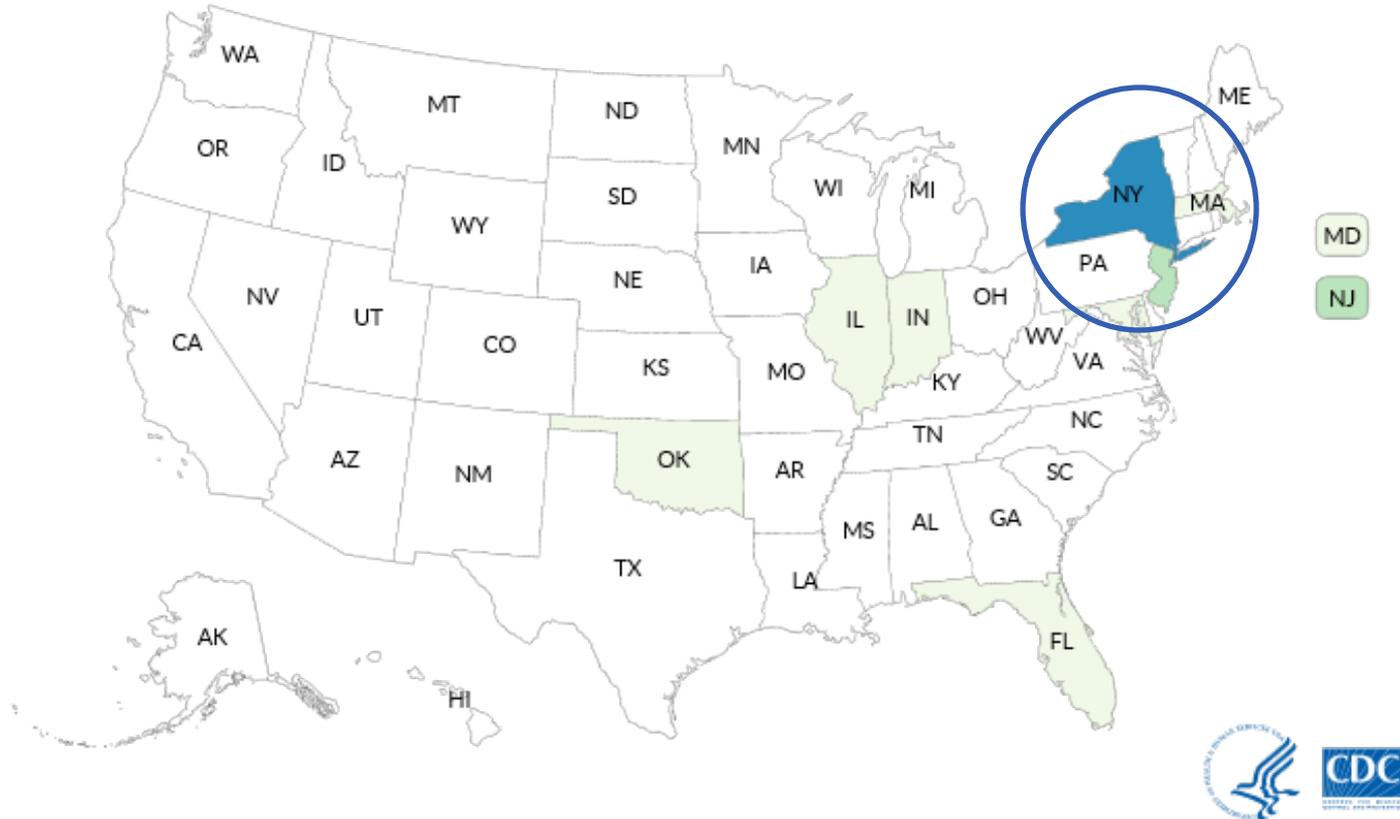
Clinical *C. auris* cases by date May 2013–May 2017 (n=86)



Epidemiologic Characteristics of US Cases

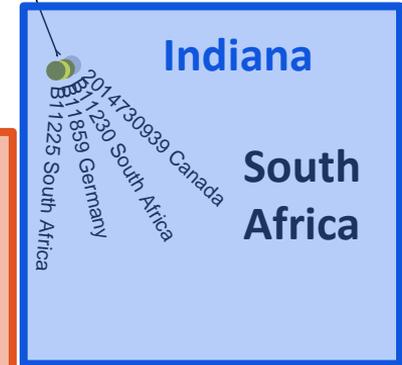
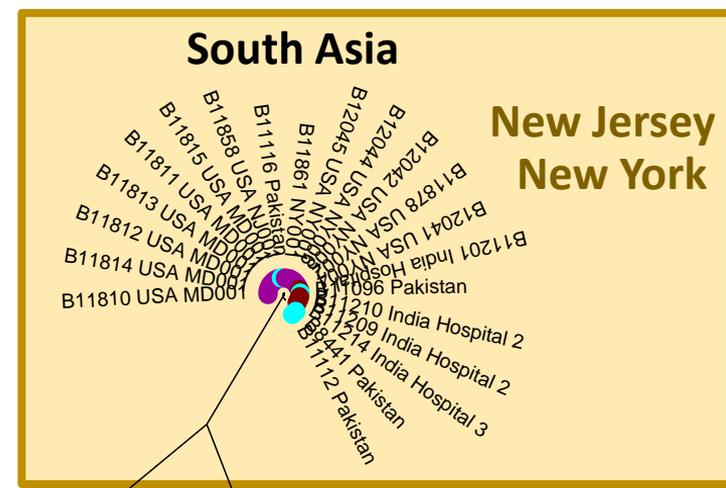
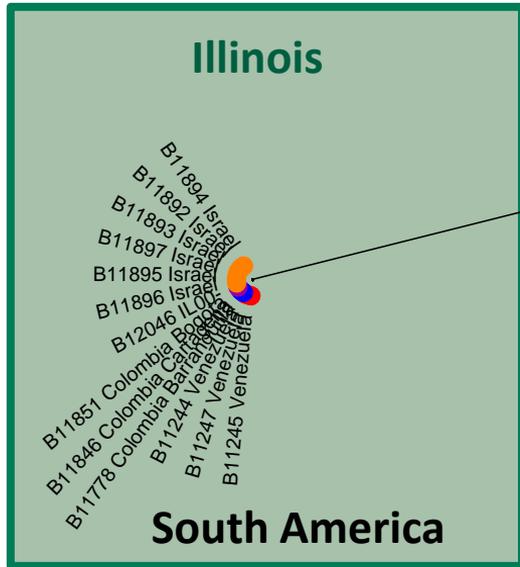
- 75% of isolates from blood
- Median age: 70, most recently, a case in a **neonate**
- Multiple underlying medical conditions and indwelling devices
 - Tracheostomy tube, central venous catheter, gastrostomy tube
- Extensive healthcare exposure (acute care hospitals, LTACHs, nursing homes with ventilator units)
- ~30% 30-day mortality

Map of US *C. auris* cases



Does the US have it's own strain?

1,000



Evidence for Transmission



Clusters at both
hospitals and
long-term care
facilities



Several
patients
received care
at same
hospital



Several
patients at
same long-
term acute
care hospital

Three cases with recent travel

- Patient transferred directly from a South African hospital with *C. auris* wound infection.
- Patient with *C. auris* in the urine in 2017; look back revealed he was transferred directly from a Venezuelan hospital with *C. auris* BSI in 2015.
- Patient with recent history of hospitalization in Pakistan, had +urine culture with *C. auris*.

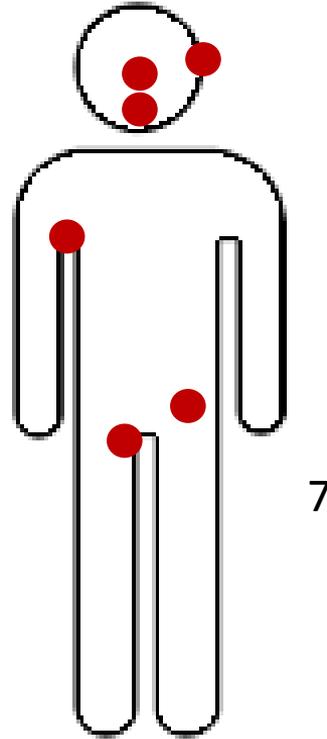


**Multiple introductions of *C. auris*
followed by local transmission**

Transmission of Candida?



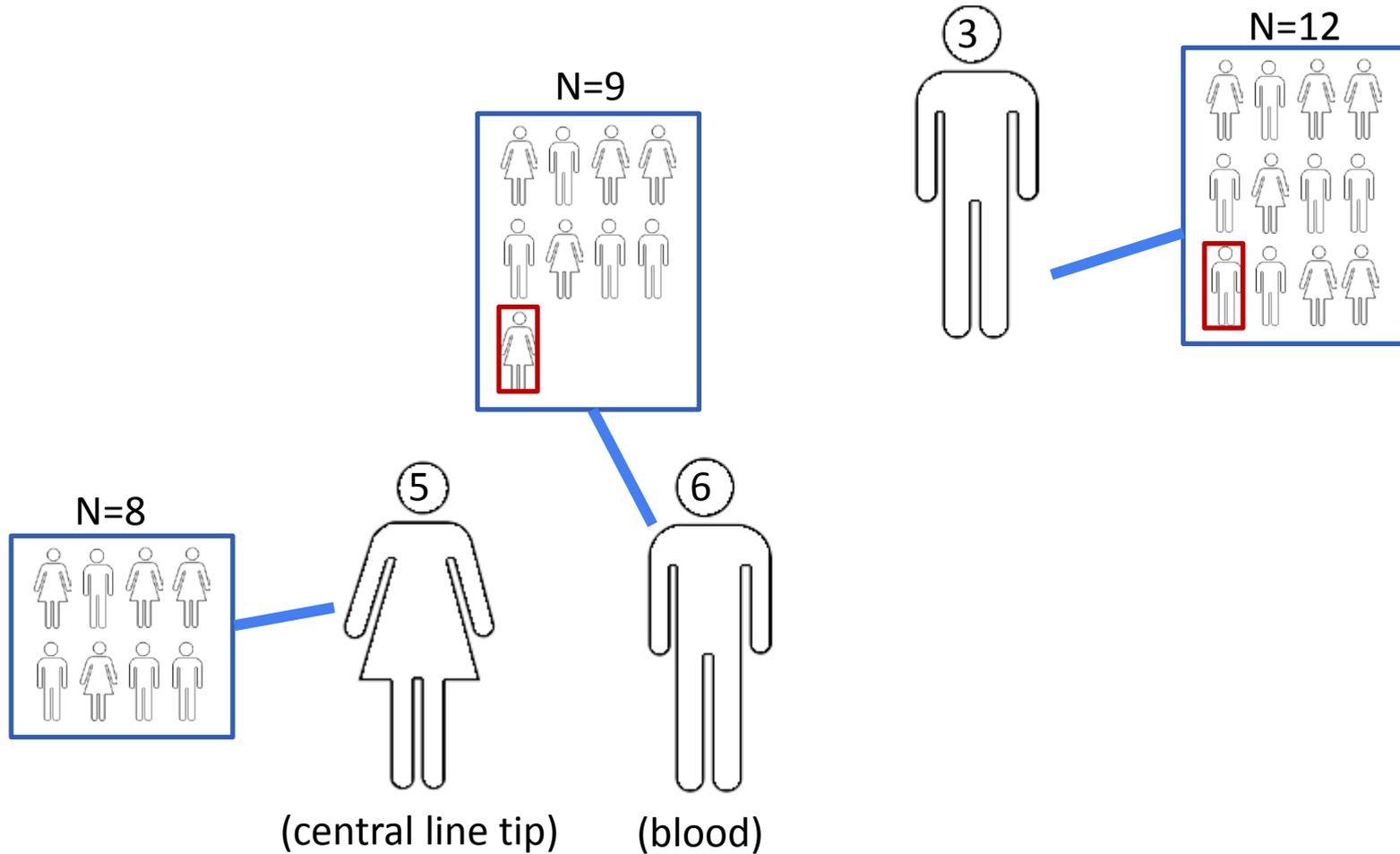
C. auris colonizes skin and other body sites



C. auris found on multiple surfaces in rooms



Close contacts get colonized with *C. auris*



What Could Account for Transmission?

- Colonizes patients (and colonized patients are asymptomatic—so can go undetected)
- Persists for >4 weeks on plastic surfaces
- Quaternary ammonium compounds inadequate for disinfection



United States antifungal resistance

- Illinois
 - Pan susceptible
- New Jersey
 - All fluconazole resistant, one echinocandin resistant, some amphotericin B resistant
- New York
 - All fluconazole resistant, one echinocandin resistant, some amphotericin B resistant
- Oklahoma
 - Fluconazole and echinocandin resistant

Is it truly an MDR organism?

- MICs for 340 isolates collected worldwide
- 75% of isolates resistant to at least one class of antifungal
- 20% of isolates resistant to two classes of antifungal
- 3 isolates pan resistant



A Paradigm Shift in thinking about *Candida* infections

- Capable of serious infections
- Antifungal resistance is the norm
- Thrives on skin
- Contaminates the environment

CAN SPREAD IN HEALTHCARE SETTINGS



Controlling the spread of *C. auris*



IDENTIFY



TREAT



INFECTION CONTROL



Challenges with identification

- *C. auris* can be misidentified as

Candida haemulonii

- *Candida famata*

- *Candida sake*

- *Candida catenulate*

- *Candida guilliermondii*

- *Candida lusitaniae*

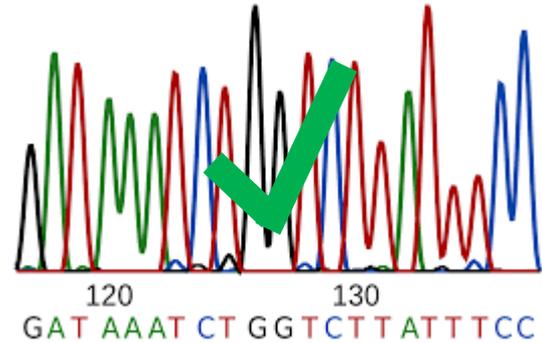
- *Rhodotorula glutinis*,

- *Candida* spp. after a validated method of *Candida* identification attempted.



C. auris can be correctly identified using MALDI-TOF and DNA sequencing

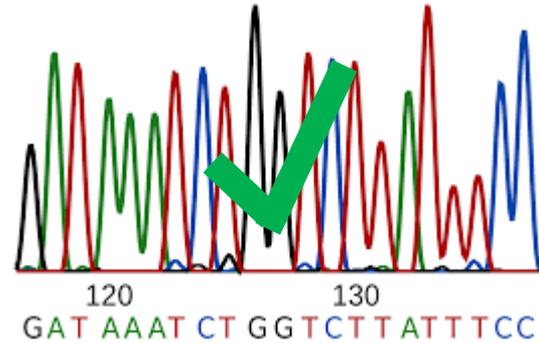
Candida auris is difficult to identify



Candida auris is difficult to identify



Ver 8.01 software



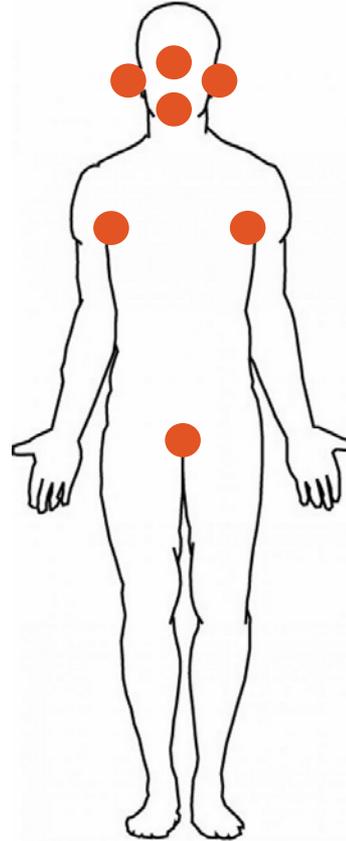
RUO with Saramis Ver 4.14

Challenges with identification

- 30% of clinical cases in the U.S. have been from non-bloodstream isolates (urine, bile, wounds, etc)
- Isolates from non-sterile sites may not be worked up species level
 - Though no treatment may be needed, infection control is needed if *C. auris*



Challenges with detecting colonized individuals

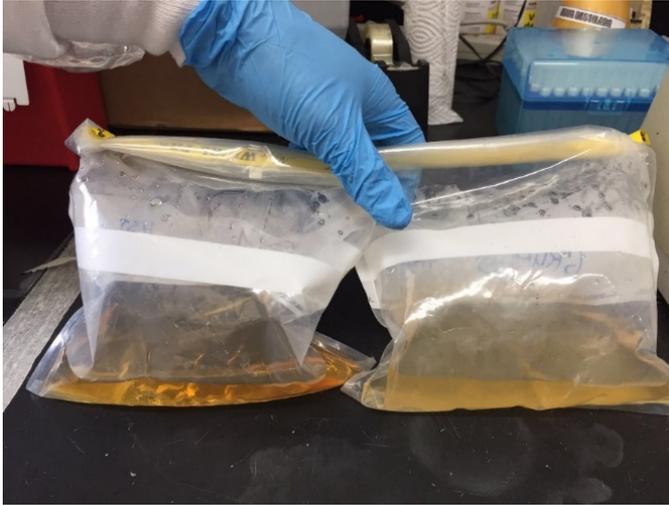


**Important because
infection control
measures are needed**

Salt Sab Dex Broth with Chloramphenicol and Gentamicin



Enrichment broth



Cloudy (right) = positive

CHROMagar



C. auris appears pink

Working with *C. auris* in the lab

At the CDC reference laboratory

- Gloves and gowns are mandatory!
- We work in a biological safety cabinet
- We clean with bleach after working with *C. auris* or a potential *C. auris*



Treatment

- Echinocandins are first line
- Resistance can be problematic
 - Some echinocandin resistant isolates
 - At least one case with documented development of echinocandin resistance on treatment
- Close monitoring of patient needed



Recommended Infection Control Practices

- Standard and Contact Precautions
- Single room
- Hand hygiene
- Daily and terminal cleaning with disinfectants with *Clostridium difficile* claim
- Contact tracing



Take home points:

Candida auris poses a unique Public Health threat

- Can be difficult to identify
- Multidrug-resistant (possibly even to all major antifungal drugs)
- Spreads in healthcare settings
- Persists in the environment

Acknowledgements CDC Mycotic Diseases

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candidaauris@cdc.gov

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- Indiana
- Oklahoma

CDC DHQP

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- Bola Ogundimu
- Janet Glowicz

Special thank you to everyone that continues to notify CDC and SPHLs about possible cases

candidaauris@cdc.gov

Thank you!

Questions?

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



Candida auris:

Surveillance and Reporting

- Be aware of [resources](#) for identifying *C. auris* and implement infection control measures to prevent spread
- Report possible *C. auris* or isolates of *C. haemulonii* and *Candida* spp. that cannot be identified after routine testing to your local health department and the HAI program, at HAIProgram@cdph.ca.gov.
- For questions regarding fungal diagnostic testing services at CDPH MDL, contact Dr. Linlin Li at Linlin.Li@cdph.ca.gov.

Questions?

The HAI Program is available for consultation. Contact us by email:

HAIProgram@cdph.ca.gov